Hedgehog signaling regulates the generation of ameloblast progenitors in the continuously growing mouse incisor.

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Public Summary:
In many organ systems such as the skin, gastrointestinal tract and hematopoietic system, homeostasis is dependent on the continuous generation of differentiated progeny from stem cells. The rodent incisor, unlike human teeth, grows throughout the life of the animal and provides a prime example of an organ that rapidly deteriorates if newly differentiated cells cease to form from adult stem cells. Hedgehog (Hh) signaling has been proposed to regulate self-renewal, survival, proliferation and/or differentiation of stem cells in several systems, but to date there is little evidence supporting a role for Hh signaling in adult stem cells. Our results revealed the existence of a positive-feedback loop in which differentiating progeny produce the signal that in turn allows them to be generated from stem cells. We intend to use the insights provided by our experiments in mice to guide us in the use of stem cells in regenerating dental tissues.

Scientific Abstract:
In many organ systems such as the skin, gastrointestinal tract and hematopoietic system, homeostasis is dependent on the continuous generation of differentiated progeny from stem cells. The rodent incisor, unlike human teeth, grows throughout the life of the animal and provides a prime example of an organ that rapidly deteriorates if newly differentiated cells cease to form from adult stem cells. Hedgehog (Hh) signaling has been proposed to regulate self-renewal, survival, proliferation and/or differentiation of stem cells in several systems, but to date there is little evidence supporting a role for Hh signaling in adult stem cells. We used in vivo genetic lineage tracing to identify Hh-responsive stem cells in the mouse incisor and we show that sonic hedgehog (SHH), which is produced by the differentiating progeny of the stem cells, signals to several regions of the incisor. Using a hedgehog pathway inhibitor (HPI), we demonstrate that Hh signaling is not required for stem cell survival but is essential for the generation of ameloblasts, one of the major differentiated cell types in the tooth, from the stem cells. These results therefore reveal the existence of a positive-feedback loop in which differentiating progeny produce the signal that in turn allows them to be generated from stem cells.